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- **12.** Henry BM. COVID-19, ECMO, and lymphopenia: a word of caution. *Lancet Respir Med.* 2020;8:e24.
- **13.** Kon ZN, Smith DE, Chang SH, et al. Extracorporeal membrane oxygenation support in severe COVID-19. *Ann Thorac Surg.* 2021;111:537-543.
- 14. Barbaro RP, MacLaren G, Boonstra PS, et al. Extracorporeal membrane oxygenation support in COVID-19: an international cohort study of the Extracorporeal Life Support Organization registry. *Lancet*. 2020;396:1071-1078. Published correction appears in *Lancet*. 2020;396:1070.
- **15.** Shih E, DiMaio JM, Squiers JJ, et al. Venovenous extracorporeal membrane oxygenation for patients with refractory coronavirus disease 2019 (COVID-19): multicenter experience of referral hospitals in a large health care system. *J Thorac Cardiovasc Surg.* 2022;163:1071-1079.e3.
- **16.** Shih E, Squiers JJ, DiMaio JM, et al. Outcomes of extracorporeal membrane oxygenation in patients with severe acute respiratory distress syndrome caused by COVID-19 versus influenza. *Ann Thorac Surg.* 2022;113:1445-1451.
- 17. Harrell F. Hmisc: Harrell Miscellaneous. R package version 4.4-2. https://CRAN.R-project.org/package=Hmisc
- 18. R Core Team. R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2019. https://www.R-project.org/
- **19.** Harrell F. rmsb: Bayesian Regression Modeling Strategies. R package version 0.0.2. 2021. https://CRAN.R-project.org/package=rmsb
- 20. Kumar PA, Hu Y, Yamamoto Y, et al. Distal airway stem cells yield alveoli in vitro and during lung regeneration following H1N1 influenza infection. Cell. 2011;147:525-538.

- 21. Kotton DN, Morrisey EE. Lung regeneration: mechanisms, applications and emerging stem cell populations. *Nat Med*. 2014;20:822-832.
- 22. Liu Q, Liu K, Cui G, et al. Lung regeneration by multipotent stem cells residing at the bronchioalveolar-duct junction. *Nat Genet*. 2019;51:728-738.
- 23. Basil MC, Katzen J, Engler AE, et al. The cellular and physiological basis for lung repair and regeneration: past, present, and future. *Cell Stem Cell*. 2020:26:482-502.
- **24.** Zimmermann M, Bein T, Arlt M, et al. Pumpless extracorporeal interventional lung assist in patients with acute respiratory distress syndrome: a prospective pilot study. *Crit Care*. 2009;13:R10.
- 25. Loyalka P, Cheema FH, Rao H, Rame JE, Rajagopal K. Early usage of extracorporeal membrane oxygenation in the absence of invasive mechanical ventilation to treat COVID-19-related hypoxemic respiratory failure. *ASAIO J.* 2021;67:392-394.
- 26. Brochard L, Slutsky A, Pesenti A. Mechanical Ventilation to Minimize Progression of Lung Injury in Acute Respiratory Failure. *Am J Respir Crit Care Med*. 2017;195:438-442. https://doi.org/10.1164/rccm.201605-1081CP
- **27.** Jacobs JP, Falasa MP, Machuca TN. Commentary: extracorporeal membrane oxygenation for patients with refractory coronavirus disease 2019: what do we know and what do we need to learn? *J Thorac Cardiovasc Surg.* 2022;163:1080-1082. https://doi.org/10.1016/j.jtcvs.2020.11.128
- 28. Bharat A, Machuca TN, Querrey M, et al. Early outcomes after lung transplantation for severe COVID-19: a series of the first consecutive cases from four countries. *Lancet Respir Med*. 2021;9:487-497. https://doi.org/10.1016/S2213-2600(21)00077-1

# Real-World Outcomes for ECMO in COVID-19



## INVITED COMMENTARY:

Extracorporeal membrane oxygenation (ECMO) is an important form of life support for the sickest patients with COVID-19-related acute respiratory distress syndrome. Initial observational studies demonstrated similar mortality rates in patients supported with ECMO for COVID-19 and non-COVID-19-related acute respiratory distress syndrome (approximately 30%-40%).1,2 Studies after the first wave suggested that mortality increased from initial estimates, with overall mortality exceeding 50%.3,4 It is important to note that these and similar studies are limited by lack of control groups and confounded by severity of illness, timing of support, ECMO delivery models, and center expertise; they are also highly selected populations. In the only unselected cohort of COVID-19 patients receiving ECMO from a countrywide German database, the mortality was 68%.4

Against this background, Hall and colleagues<sup>5</sup> report their clinical experience of 505 patients with COVID-19 at 61 US hospitals in this issue of *The Annals of Thoracic Surgery*. The mortality rate of 61% was higher than reported in numerous similar cohorts. Nevertheless, it is in keeping with the German experience.<sup>4,5</sup>

Odds of survival declined with a longer time between diagnosis of COVID-19 and endotracheal intubation, potentially bolstering the assertion that postponing invasive ventilation in patients with impending respiratory failure could worsen outcomes. Although this finding has face validity, it is confounded by uncertainty between the true onset of COVID-19 and the time of laboratory diagnosis, as well as access to testing early in the pandemic.

Comparison of existing COVID-19 studies raises the question of why such differences in outcomes exist and what the "right" mortality for COVID ECMO should be? The answer is unknowable from the current data. Even if criteria for ECMO could be standardized, data on outcomes would still be confounded by varying ECMO delivery models. Randomized clinical trials are needed to better understand the efficacy of ECMO in this population. What the present, and the German, studies show us are "real world" observational data. Hall and colleagues included both community and academic centers that reported case volumes varying from over 70 cases in the study period to fewer than 5 (with a known volume-outcome relationship with ECMO).<sup>3</sup>

Several recommendations can be made. First, where feasible, ECMO should be provided by experienced centers. This was not always possible during the pandemic. Second, centers with high mortality relative to registry data should consider being more restrictive with ECMO criteria. Similarly, low mortality rates may represent an opportunity to expand ECMO criteria. Third, although there is no consensus on the ideal ECMO delivery model, centers reporting good outcomes may

be used as benchmarks within the context of local practice constraints. Delivery models may be assessed in terms of risk-adjusted outcomes, staffing intensity, standardization, and cost, with the understanding that these exist in a matrix; optimizing one metric may be deleterious to another. Ultimately, absent well-conducted randomized trials, quality in ECMO will likely follow patterns found in delivery of other technologies and will improve by bringing collective local attention to the clinical challenge.

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### REFERENCES

- Schmidt M, Hajage D, Lebreton G, et al. Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome associated with COVID-19: a retrospective cohort study. *Lancet Respir Med*. 2020;8:1121-1131.
- 2. Barbaro RP, MacLaren G, Boonstra PS, et al. Extracorporeal Life Support Organization. Extracorporeal membrane oxygenation support in COVID-19: an international cohort study of the Extracorporeal Life Support Organization registry. *Lancet*. 2020;396:1071-1078.
- 3. Barbaro RP, MacLaren G, Boonstra PS, et al. Extracorporeal Life Support Organization. Extracorporeal membrane oxygenation for COVID-19: evolving outcomes from the international Extracorporeal Life Support Organization Registry. *Lancet*. 2021;398:1230-1238.
- **4.** Karagiannidis C, Slutsky AS, Bein T, et al. Complete countrywide mortality in COVID patients receiving ECMO in Germany throughout the first three waves of the pandemic. Crit. Care. 2021;25:413.
- 5. Hall CA, Jacobs JP, Stammers AH, et al. Multi-institutional analysis of 505 patients with coronavirus disease-2019 supported with extracorporeal membrane oxygenation: predictors of survival. *Ann Thorac Surg.* 2022;114: 61-69.